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EXAMINER	
CROW, ROBERT THOMAS	
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NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/501,772	BOCKELMANN ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 27 August 2009 in which claim 1 was amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 112, first paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1-17 are under prosecution.

2. The following rejections are new rejections necessitated by the amendments.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-9 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lindsay et al (U.S. Application Publication No. US 2004/0238379 A1, filed 7 August 2002) in view of Kariyone et al (U.S. Patent No. 5,242,793, issued 7 September 1993) in view of Hafeman et al (U.S. Patent No. 5,164,319, issued 17 November 1992).

Regarding claims 1 and 11, Lindsay et al teach a method for detecting at least one parameter representative of molecule proves fixed to active zones of a sensor in the form of a genechip comprising a plurality (i.e., network) of field effect transistors (paragraph 0040), wherein each field effect transistor (i.e., FET) has a source region, gain region, and a drain region (paragraph 0028), which forms an active zone on which the parameter is detected. Lindsay et al further teach bringing some of said active zones into contact with molecular probes in order to fix said probes; namely, DNA, which is a molecular probe, is injected into a genechip having a plurality of FETS each having a difference nucleic acid sequence thereon (paragraph 0040). The DNA is in a buffer (paragraphs 0037 and 0032), which is an electrolyte solution. Because the electrolyte solution is injected into the genechip having the plurality of FETs (paragraph

0040 and 0037), the active zones are bathed in the electrolyte solution. Lindsay et al also teach measuring at least on point of a drain current characteristic to detect (i.e., deduce) the representative parameter by comparison between at least two measurements obtained for two different active zones immerged in the electrolyte solution; namely, drain current is measured to detect fixing of the probe to a FET via hybridization (i.e., the representative parameter; paragraph 0018 and Figure 7), wherein a plurality of FETS (i.e., at least two) including a control FET are measured and compared (paragraph 0040).

While Lindsay et al teach the detection of an organic monolayer on the surface of the FETs (paragraph 0031), Lindsay et al do not explicitly teach initial detection of the immobilization of a probe (i.e., a first organic layer) before detection of the hybridization of targets to the probes (i.e., binding of a target, which is a second organic layer, to the first organic layer).

However, Kariyone et al teach the immobilization of a probe, in the form of an enzyme, on an electrode, wherein electrical measurements are made to detect the presence of the immobilized probe (i.e., claims 1 and 11), which has the added advantage of confirming the stable immobilization of the probe to the surface (column 17, lines 1-10), thereby providing a quality control indicator for a sensor (i.e., an individual electrode). Thus, Kariyone et al teach the known technique of measuring initial immobilization of a probe to a surface of a sensor.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Lindsay

to further comprise the initial detection of the immobilization of a probe as taught by Kariyone et al to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of providing a quality control indicator for each of the sensors of the method as a result of confirming the stable immobilization of the probe to the surface as explicitly taught by Kariyone et al (column 17, lines 1-10). In addition, it would have been obvious to the ordinary artisan that the known technique of using the initial detection of the immobilization of a probe as taught by Kariyone et al could have been applied to the method of Lindsay et al with predictable results because the known technique of using the initial detection of the immobilization of a probe as taught by Kariyone et al predictably results in verification of stably immobilized probes.

While Lindsay et al teach one of the immerged FETs is a control FET (i.e., not used for hybridization; paragraph 0040), neither Lindsay et al nor Kariyone et al teach fixing the potential of the active zones with an electrode that applies a gate source voltage to the FETs.

However, Hafeman et al teach a method wherein a plurality of electrodes (i.e., pixel elements; column 2, lines 25-52) is used to detect an analyte in a fluid (Abstract). The method further comprises the use of a single controlling electrode (i.e., counter electrode; column 2, lines 20-25) which has a fixed potential that sets the potential of the other electrodes, thereby providing the added advantage of allowing measurement of analyte binding (column 19, line 45-column 20, line 15) with maximal sensitivity

(Abstract). Thus, Hafeman et al teach the known technique of fixing the potential of the active zones with a common electrode.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Lindsay in view of Kariyone et al so that the potential of the active zones is fixed with a common electrode as taught by Hafeman et al. Application of the fixed potential in accordance with the teachings of Hafeman et al would result in the application of a gate source voltage to the field effect transistors of Lindsay et al in view of Kariyone et al, thus arriving at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage allowing the binding event to be measured with maximal sensitivity as explicitly taught by Hafeman et al (column 19, line 45-column 20, line 15 and Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of fixing the potential of the active zones with a common electrode as taught by Hafeman et al could have been applied to the method of Lindsay et al in view of Kariyone et al with predictable results because the known technique of fixing the potential of the active zones with a common electrode as taught by Hafeman et al predictably results in a reliable method for detection of binding on the transistors.

Regarding claim 2, the method of claim 1 is discussed above. Lindsay et al also teach said measuring comprises applying a voltage between the drain region and source region (paragraph 0010) and the application of a drain current (paragraph 0018

and Figure 7). Thus, modification of the method of Lindsay et al in view of Kariyone et al and Hafeman et al results in the measuring of the fixing of the probes via the application of voltage and drain currents as detailed above.

Regarding claim 3, the method of claim 1 is discussed above. While Lindsay et al also teach rinsing of sensors before taking measurements (paragraph 0005), Lindsay et al do not specifically teach the rinsing step is between contacting the array with the probes and bathing with the electrolyte solution. However, the courts have held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). See MPEP 2144.04 IV.C.

Regarding claim 4, the method of claim 1 is discussed above. Lindsay et al further teach rinsing with an electrolyte solution (i.e., comprising a non-hybridizing target) before adding a solution containing target molecules capable of interacting specifically with the molecular probes, then taking a measurement (paragraphs 0036-0039),

Regarding claims 5-6, the method of claim 1 is discussed above. Lindsay et al teach adding an electrolyte solution containing target molecules capable of interacting specifically with the molecular probes; namely, a solution containing target molecules capable of interacting specifically with the molecular probes wherein the solution is a buffer (paragraphs 0036-0039), and is thus an electrolyte solution. Lindsay et al also teach subsequently taking a measurement (paragraphs 0036-0039), wherein said measuring comprises applying a voltage between the drain region and source region

(paragraph 0010) and the application of a drain current (paragraph 0018 and Figure 7). The measurement deduces the representative parameter by comparison between at least two measurements obtained for two different active zones immerged in the electrolyte solution; namely, drain current is measured to detect fixing of the probe to a FET via hybridization (i.e., the representative parameter; paragraph 0018 and Figure 7), wherein a plurality of FETS (i.e., at least two) including a control FET are measured and compared (paragraph 0040).

Regarding claim 7, the method of claim 5 is discussed above. Lindsay et al also teach using a plurality of measurement of at least one point of the characteristic, which are spaced out over time; namely, the operation of the FETs is plotted over time (paragraph 0036). Plotting over time comprises taking a plurality of spaced out measurements.

Regarding claim 8, the method of claim 1 is discussed above. Lindsay et al further teach said comparison is carried out by differential measurements (paragraph 0032).

Regarding claim 9, the method of claim 1 is discussed above. Lindsay et al teach the comparison is carried out between measurements carried out on at least two transistors corresponding to said active zones after which are bathed in said electrolyte solution after having been brought into contact with said molecular probes; namely, the genechip has a plurality of FETS each having a difference nucleic acid sequence thereon (paragraph 0040). The DNA is in a buffer (paragraphs 0037 and 0032), which is an electrolyte solution. Because the electrolyte solution is injected into the genechip

having the plurality of FETs (paragraph 0040 and 0037), the active zones are bathed in the electrolyte solution. Lindsay et al also teach measuring at least on point of a drain current characteristic to detect (i.e., deduce) the representative parameter by comparison between at least two measurements obtained for two different active zones immerged in the electrolyte solution; namely, drain current is measured to detect fixing of the probe to a FET via hybridization (i.e., the representative parameter; paragraph 0018 and Figure 7), wherein a plurality of FETS (i.e., at least two) including a control FET are measured and compared (paragraph 0040). Because the FETs are measured after addition of the electrolyte (i.e., buffer), the measurements are carried out on said active zones which are bathed in said electrolyte solution.

Regarding claim 12, the method of claim 1 is discussed above. Lindsay et al teach the probes are DNA (paragraph 0039).

6. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lindsay et al (U.S. Application Publication No. US 2004/0238379 A1, filed 7 August 2002) in view of Kariyone et al (U.S. Patent No. 5,242,793, issued 7 September 1993) in view of Hafeman et al (U.S. Patent No. 5,164,319, issued 17 November 1992) as applied to claim 1 above, and further in view of Hashimoto (U.S. Patent Application Publication No. US 2001/0024788 A1, published 27 September 2001).

Regarding claim 10, the method of claim 1 is discussed above in Section 5.

While Lindsay et al teach one active zone (i.e., the control zone) does not have probes thereon (paragraphs 0036-0040), neither Lindsay et al, Kariyone et al, nor

Hafeman et al teach bathing both zones in the same electrolyte solution after one zone is contacted with molecular probes and the second zone is not contacted with molecular probes.

However, Hashimoto teaches spotting of nucleic acids directly on the electrodes, followed by drying (i.e., before use; paragraph 0049). Thus, Hashimoto teaches the functionally equivalent technique of spotting nucleic acids on electrodes and drying the spots before use.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method wherein probes are immobilized on some, but not all, transistors as taught by Lindsay et al in view of Kariyone et al and Hafeman et al with the functionally equivalent method of immobilizing probes on electrodes by spotting and drying as taught by Hashimoto to arrive at the instantly claimed method with a reasonable expectation of success. The modification would result in spotting probes on those transistors that have probes, but not on the control transistor; thus, one transistor (which is an active zone) has not been brought into contact with said probes. The modification of Hashimoto would also result in drying of the zones before use; thus, when comparison of the measurements is made, all of the transistors are bathed in the same electrolyte solution during the measurements. In addition, the modification taught by Hashimoto could be applied to the method of Lindsay et al in view of Kariyone et al and Hafeman et al with predictable results because the modification of Hashimoto predictably results in a functionally equivalent method of fixing probes on surfaces (i.e., the transistors).

7. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lindsay et al (U.S. Application Publication No. US 2004/0238379 A1, filed 7 August 2002) in view of Kariyone et al (U.S. Patent No. 5,242,793, issued 7 September 1993) in view of Hafeman et al (U.S. Patent No. 5,164,319, issued 17 November 1992) as applied to claims 1 and 12 above, and further in view of Price (U.S. Patent No. 5,805,014, issued 8 September 1998).

Regarding claim 13, the method of claims 1 and 12 is discussed above in Section 5.

While Lindsay et al teach the FETs that are depleted (paragraph 0027) and n-channel type (paragraph 0021), neither Lindsay et al, Kariyone et al, nor Hafeman et al explicitly teach depleted n-channel type FETs with a negative gate bias.

However, Price teaches FETs in the form of depleted n-channel MOSFETs having a negative gate bias, which has the added advantage of providing a circuit that maintains the efficiency of a power supply by drawing minimal power (column 1, lines 55-67). Thus, Price teaches the known technique of using depleted n-channel MOSFETs having a negative gate bias.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising depleted and n-channel type FETs as taught by Lindsay et al in view of Kariyone et al and Hafeman et al so that the FETs are the depleted n-channel type FETs with a negative gate bias as taught by Price to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the

modification because said modification would have resulted in a method having the added advantage of providing a circuit that maintains the efficiency of a power supply by drawing minimal power as explicitly taught by Price (column 1, lines 55-67). In addition, it would have been obvious to the ordinary artisan that the known technique of using the depleted n-channel type FETs with a negative gate bias of Price could have been applied to the method of Lindsay et al in view of Kariyone et al and Hafeman et al with predictable results because the known technique of using depleted n-channel type FETs with a negative gate bias of Price predictably results in FETs that are functionally equivalent to the FETs of Lindsay et al in view of Kariyone et al.

8. Claims 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lindsay et al (U.S. Application Publication No. US 2004/0238379 A1, filed 7 August 2002) in view of Kariyone et al (U.S. Patent No. 5,242,793, issued 7 September 1993) in view of Hafeman et al (U.S. Patent No. 5,164,319, issued 17 November 1992) as applied to claims 1 and 12 above, and further in view of Hollis et al (U.S. Patent No 5,653,939, issued 5 August 1997), Dryja et al (U.S. Patent No. 5,498,521, issued 12 March 1996), and Blackburn (U.S. Patent Application No. US 2003/0190608 A1, filed 17 May 2001).

Regarding claims 14 and 15, the method of claims 1 and 12 is discussed above in Section 5.

Lindsay et al teach comparing the signals of multiple zones; namely, different sequences on different FETs are compared to control zones (paragraph 0040).

Neither Lindsay et al, Kariyone et al, nor Hafeman et al explicitly teach two zones (i.e., array locations) for detecting two different DNA samples (i.e., claim 14).

However, Hollis et al teach a plurality of zones in the form of a plurality of test sites comprising electrodes having different nucleotide sequences thereon for simultaneous detection of a plurality of different targets (column 4, lines 35-50). The targets are simultaneously added to the array in an electrolyte solution (column 4, lines 35-50), thereby bathing all zones in a solution comprising solutions obtained from two different samples. It is noted that the claim does not require the two solutions to only bathe one zone; thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). Hollis et al also teach the method compares the sample by simultaneously screening large numbers of polymorphic market of an individual, thereby aiding in the study of genetic diseases and the development of therapeutics (column 17, lines 1-16). Thus, Hollis et al teach the known technique of using two zones for detecting two different DNA samples.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Lindsay et al in view of Kariyone et al and Hafeman et al so that two zones are used to detect two different DNA samples as taught by Hollis et al to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of aiding in the study of genetic diseases and

the development of therapeutics as explicitly taught by Hollis et al (column 17, lines 1-16). In addition, it would have been obvious to the ordinary artisan that the known technique of using two zones for detecting two different DNA samples of Hollis et al could have been applied to the method of Lindsay et al in view of Kariyone et al and Hafeman et al with predictable results because the known technique of using two zones for detecting two different DNA samples of Hollis et al predictably results in detection of disease related genetic markers.

Neither Lindsay et al, Kariyone et al, Hafeman et al, nor Hollis et al teach enzymological reactions performed on two samples produced from different patients (i.e., claim 15).

However, Dryja et al teach samples from several patients (i.e., claim 15) assayed by the same PCR reaction, which is an enzymological reaction, which has the added advantage of aiding in the determination of a single point mutant responsible for a genetic disease (column 6, line 65-column 7, line 15). Thus, Dryja et al teach the known technique of using enzymological reactions and two samples produced from different patients (i.e., claim 15).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Lindsay et al in view of Kariyone, Hafeman et al, and Hollis et al with using enzymological reactions and two samples produced from different patients (i.e., claim 15) of Dryja et al to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said

modification would have resulted in a method having the added advantage of aiding in the determination of a single point mutant responsible for a genetic disease as explicitly taught by Dryja et al (column 6, line 65-column 7, line 15). In addition, it would have been obvious to the ordinary artisan that the known technique of using the method steps of Dryja et al could have been applied to the method of Lindsay et al in view of Kariyone et al, Hafeman et al, and Hollis et al with predictable results because the known technique of using the method steps of Dryja et al predictably result in detection of disease related genetic markers.

Neither Lindsay et al, Kariyone et al, Hafeman et al, Hollis et al, nor Dryja et al teach the enzymological reaction is performed in each zone (i.e., claim 14).

However, Blackburn teaches a method utilizing a microchip having a plurality of zones in the form of a plurality of wells, wherein separate enzymological reactions in the form of PCR reactions are performed in each zone, which has the added advantage of allowing parallel independently controlled molecular reactions to be performed and optimized (paragraph 0272). Thus, Blackburn teaches the known technique of performing an enzymological reaction in each of the zones.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of enzymological reactions and specific zones as taught by Lindsay et al in view of Kariyone, Hafeman et al, Hollis et al, and Dryja et al so that the enzymological reactions are each performed in a respective zone as taught by Blackburn to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would

have been motivated to make the modification because said modification would have resulted in a method having the added advantage of allowing parallel independently controlled molecular reactions to be performed and optimized as explicitly taught by Blackburn (paragraph 0272). In addition, it would have been obvious to the ordinary artisan that the known technique of performing an enzymological reaction in each of the zones as taught by Blackburn could have been applied to the method of Lindsay et al in view of Kariyone et al, Hafeman et al, Hollis et al, and Dryja et al with predictable results because the known technique of performing an enzymological reaction in each of the zones as taught by Blackburn in a reliable method of independently amplifying an analyte sample.

9. Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lindsay et al (U.S. Application Publication No. US 2004/0238379 A1, filed 7 August 2002) in view of Kariyone et al (U.S. Patent No. 5,242,793, issued 7 September 1993) in view of Hafeman et al (U.S. Patent No. 5,164,319, issued 17 November 1992) as applied to claims 1 and 12 above, and further in view Hollis et al (U.S. Patent No 5,653,939, issued 5 August 1997), Sorenson (U.S. Patent No. 5,496,699, issued 5 March 1996), and Blackburn (U.S. Patent Application No. US 2003/0190608 A1, filed 17 May 2001).

It is noted that while claim 14 is rejected above in Section 8, claim 14 is also obvious using the alternate interpretation detailed below.

Regarding claims 14 and 16, the method of claims 1 and 12 is discussed above in Section 5.

Lindsay et al teach comparing the signals of multiple zones; namely, different sequences on different FETs are compared to control zones (paragraph 0040).

Neither Lindsay et al, Kariyone et al, nor Hafeman et al explicitly teach two zones (i.e., array locations) for detecting two different DNA samples (i.e., claim 14).

However, Hollis et al teach a plurality of zones in the form of a plurality of test sites comprising electrodes having different nucleotide sequences thereon for simultaneous detection of a plurality of different targets (column 4, lines 35-50). The targets are simultaneously added to the array in an electrolyte solution (column 4, lines 35-50), thereby bathing all zones in a solution comprising solutions obtained from two different samples. It is noted that the claim does not require the two solutions to only bathe one zone; thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification. Hollis et al also teach the method compares the sample by simultaneously screening large numbers of polymorphic market of an individual, thereby aiding in the study of genetic diseases and the development of therapeutics (column 17, lines 1-16). Thus, Hollis et al teach the known technique of using two zones for detecting two different DNA samples.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Lindsay et al in view of Kariyone et al and Hafeman et al so that two zones are used to detect two different DNA samples as taught by Hollis et al to arrive at the instantly claimed

method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of aiding in the study of genetic diseases and the development of therapeutics as explicitly taught by Hollis et al (column 17, lines 1-16). In addition, it would have been obvious to the ordinary artisan that the known technique of using two zones for detecting two different DNA samples of Hollis et al could have been applied to the method of Lindsay et al in view of Kariyone et al and Hafeman et al with predictable results because the known technique of using two zones for detecting two different DNA samples of Hollis et al predictably results in detection of disease related genetic markers.

Lindsay et al in view of Kariyone et al, Hafeman et al, and Hollis et al do not teach enzymological reactions or the same patient producing two samples having the absence and the presence of a mutation (i.e., claim 16).

However, Sorenson teaches a single patient providing two samples; namely, a patient's tumor DNA is subjected to a battery of allele specific primers and PCR (column 9, lines 40-60) which is at least a first and second enzymological reaction, which produces DNA products from each reaction, and wherein the reactions produce a DNA product in the absence of a mutation and a product in the presence of a mutation (i.e., claim 16). Sorenson also teaches the method has the added advantage of allowing quantitation of mutations in patient sequences (column 9, lines 40-60). Thus, Sorenson teaches the known technique of using enzymological reactions and the same patient

producing two samples having the absence and the presence of a mutation (i.e., claim 16).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Lindsay et al in view of Kariyone, Hafeman et al, and Hollis et al with using enzymological reactions and the same patient producing two samples having the absence and the presence of a mutation (i.e., claim 16) of Sorenson to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of allowing quantitation of mutations in patient sequences as explicitly taught by Sorenson (column 9, lines 40-60). In addition, it would have been obvious to the ordinary artisan that the known technique of using the method steps of Sorenson could have been applied to the method of Lindsay et al in view of Kariyone et al, Hafeman et al, and Hollis et al with predictable results because the known technique of using the method steps of Sorenson predictably results in detection of disease related genetic markers.

Neither Lindsay et al, Kariyone et al, Hafeman et al, Hollis et al, nor Sorenson teach the enzymological reaction is performed in each zone (i.e., claim 14).

However, Blackburn teaches a method utilizing a microchip having a plurality of zones in the form of a plurality of wells, wherein separate enzymological reactions in the form of PCR reactions are performed in each zone, which has the added advantage of allowing parallel independently controlled molecular reactions to be performed and

optimized (paragraph 0272). Thus, Blackburn teaches the known technique of performing an enzymological reaction in each of the zones.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of enzymological reactions and specific zones as taught by Lindsay et al in view of Kariyone, Hafeman et al, Hollis et al, and Sorenson so that the enzymological reactions are each performed in a respective zone as taught by Blackburn to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of allowing parallel independently controlled molecular reactions to be performed and optimized as explicitly taught by Blackburn (paragraph 0272). In addition, it would have been obvious to the ordinary artisan that the known technique of performing an enzymological reaction in each of the zones as taught by Blackburn could have been applied to the method of Lindsay et al in view of Kariyone et al, Hafeman et al, Hollis et al, and Sorenson with predictable results because the known technique of performing an enzymological reaction in each of the zones as taught by Blackburn in a reliable method of independently amplifying an analyte sample.

10. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lindsay et al (U.S. Application Publication No. US 2004/0238379 A1, filed 7 August 2002) in view of Kariyone et al (U.S. Patent No. 5,242,793, issued 7 September 1993) in view of Hafeman et al (U.S. Patent No. 5,164,319, issued 17 November 1992) as applied to claim 1 above, and further in view of Anderson et al (U.S. Patent No. 5,922,591, issued 13 July 1999).

Regarding claim 17, the method of claim 1 is discussed above in Section 5.

While Lindsay et al teach a buffer solution is injected into a genechip having a plurality of FETS each having a difference nucleic acid sequence thereon (paragraph 0040), and while Hafeman et al teach a solution (i.e., an analyte fluid) is introduced into a channel (Figure 1 and column 3, lines 15-30), neither Lindsay et al, Kariyone et al, nor Hafeman et al teach a solution is circulated through the microfluidic channel to bring the solution into contact with at least one of the FETs.

However, Anderson et al teach a method comprising using a microfluidic device having an array of fixed probes in a chamber therein having a microfluidic channel (column 2, lines 20-45), wherein fluids are recirculated through the chamber, which has the added advantage of aiding in the mixing of samples and reagents used in the method (column 36, lines 10-40). Thus, Anderson et al teach the known technique of circulating a fluid through a microfluidic channel to bring the solution into contact with immobilized probes.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising FET

immobilized probes as taught by Lindsay et al in view of Kariyone et al and Hafeman et al so that the fluid is circulated through a microfluidic channel to bring the solution into contact with immobilized probes as taught by Anderson et al to arrive at the instantly claimed method with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of aiding in the mixing of samples and reagents used in the method as explicitly taught by Anderson et al (column 36, lines 10-40). In addition, it would have been obvious to the ordinary artisan that the known technique of using the circulation of a fluid through a microfluidic channel to bring the solution into contact with immobilized probes as taught by Anderson et al could have been applied to the method of Lindsay et al in view of Kariyone et al and Hafeman et al with predictable results because the known technique of circulating a fluid through a microfluidic channel to bring the solution into contact with immobilized probes as taught by Anderson et al predictably results in reliable mixing of reagents used in chip-based assays.

Response to Arguments

11. Applicant's arguments filed 27 August 2009 (hereafter the “Remarks”) have been fully considered but they are not persuasive for the reasons discussed below.

A. It is noted that the arguments presented in the Remarks refer to the previous rejections of the claims. While this Office Action presents new ground(s) of

rejection necessitated by the amendments, the arguments that are relevant to the instant rejections are considered below.

B. Applicant argues on page 9 of the Remarks that Applicant's invention offers advantages over the background art, including reduced noise, based on pages 6-7 if the instant specification.

However, the embodiments described on pages 6-7 of the specification require each of the following:

I. An Ag/AgCl electrode;

II. An Si/SiO2 interface;

III. An ISFET;

The instant claims do not require any of these specific limitations.

In addition, Hafeman et al specifically state that the methods used therein reduce background noise ((column 1, lines 35-45). Thus, the alleged advantage of the claimed invention is taught by the prior art.

Further, Applicant has provided no evidence to support this assertion because ages 6-7 of the instant specification do not show any comparison to any prior art method to establish the alleged advantages. MPEP 716.01(c) makes clear that "[t]he arguments of counsel cannot take the place of evidence in the record" (*In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)). Thus, Applicant's mere arguments regarding the alleged advantages cannot take the place of evidence in the record.

C. Applicant argues on page 12 of the Remarks that Kariyone et al do not teach detection of the fixing of molecule probes on a sensor.

However, as noted in the rejections above, Kariyone et al teach the immobilization of a probe, in the form of an enzyme, on an electrode, wherein electrical measurements are made to detect the presence of the immobilized probe (i.e., claims 1 and 11), which has the added advantage of confirming the stable immobilization of the probe to the surface (column 17, lines 1-10), thereby providing a quality control indicator for a sensor (i.e., an individual electrode). Thus, Kariyone et al teach the known technique of measuring initial immobilization of a probe to a surface of a sensor, and the modification would be obvious for the reasons stated above.

D. Applicant's remaining arguments refer to the previous rejections of the claims. These arguments have been considered but are moot in view of the new ground(s) of rejection necessitated by the amendments.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

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